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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/366,081	08/02/99	BRENNER S	802-04RE

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EXAMINER	
SHIBUYA,M	
ART UNIT	**PAPER NUMBER**
1635	14

DATE MAILED: 04/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE COPY

Office Action Summary	Application No. 09/366,081	Applicant(s) BRENNER
	Examiner Mark L. Shibuya	Group Art Unit 1635

☒ Responsive to communication(s) filed on *Feb 10, 2001*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-6 and 8-13* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *1-4 and 9-13* is/are allowed.

☒ Claim(s) *5, 6, and 8* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Raw Sequence Listing Error Report

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 2/10/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/366,081 is acceptable and a CPA has been established. An action on the CPA follows.

Response to Arguments

2. The applicants' response filed 2/10/01, has been considered. Rejections and/or objections not reiterated from the previous office action mailed 8/16/00, are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Reissue Applications

3. Applicant is reminded that the original patent, or an affidavit or declaration as to loss or inaccessibility of the original patent, must be received before this reissue application can be allowed. See 37 CFR 1.178.

Nucleotide and/or Amino Acid Sequence Disclosure

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): The copy of the "Sequence Listing" in computer readable form has not been

submitted in proper form as required by 37 C.F.R. 1.821(e) and as explained in the **attached Raw**

Applicant must provide:

a. A *corrected* computer readable form (CRF) copy of the "Sequence Listing".

b. A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

5. Applicants disclose nucleotide sequences in the specification that appear to be erroneously identified by a SEQ ID number. This must be corrected pursuant to 37 CFR 1.821(d), which states: "Where the description or claims of a patent application discuss a sequence listing that is set forth in the 'Sequence Listing' in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application." These erroneously identified SEQ ID numbers have been introduced by applicant's amendments to the specification, filed 2/10/01. For example, SEQ ID NO: 9, SEQ ID NO: 10, and SEQ ID NO: 17, do not recite the same sequences as found in column 23, lines 64-67, even though the specification was so amended, (applicant's response, filed 2/10/01, at p. 2, paragraph 3). In that particular situation, the specification refers to "words" (W_x) whose definitions (*i.e.*, nucleotide sequences) are to be found in Table I in column 7. However, "spelling out" the nucleotide sequences of these "words" does not yield the sequences of SEQ ID NOs: 9, 10, and 17. The examiner would like to emphasize that similar problems extend throughout the instant

amendments to the specification, which were drawn to address the aforementioned nucleotide sequence compliance rules. Therefore, these problems extend to applicant's other amendments of the specification in said response, *all of which must be corrected. See, also* the below objection to the Specification.

6. In applicant's Declaration Concerning Sequence Listing Under 37 C.F.R. 1.82(f), filed 2/10/01, applicant appears to not have included a statement that the content of the paper and computer readable copies are the same and, where applicable, include **no new matter**, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

7. Applicant is required to comply with the corrections for the sequence listing and/or computer readable form, and specification as per above as part of a complete response to this official action.

Information Disclosure Statement

8. The information disclosure statement filed 5/17/01 by *fax* fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. The IDS states: "Copies of the cited references are enclosed or have been previously submitted in prior applications(s) to the above application." As stated, the examiner finds no enclosed copies of references. If the cited references were previously submitted in prior

applications, the examiner would appreciate a statement to that effect, along with citations of the applications in which the references are to be found.

Specification

9. The amendment filed 2/10/01 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

a. Applicant's amendments to the specification, filed 2/10/01, including the new Sequence Listing introduce sequences for which no support may in be found in the specification as filed. For example, SEQ ID NO: 9, SEQ ID NO: 10, and SEQ ID NO: 17, do not recite the same sequences as found in column 23, lines 64-67, even though the specification was so amended, (applicant's response, filed 2/10/01, at p. 2, paragraph 3). These problems extend to applicant's other amendments of the specification in said response. In order to overcome the instant objection, applicant must point with particularity as to where support for said amendments to the specification are to be found in the specification as originally filed. *See, also* the above objection to the Nucleotide and/or Amino Acid Sequence Disclosure.

b. Applicant is required to cancel the new matter in the reply to this Office action.

Claim Rejections - 35 U.S.C. § 102

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Wang, EP 0304845 A2 (published 3/1/1989).

a. Claim 5 recites a composition of matter comprising a plurality of polynucleotides selected from cDNA molecules or fragments of a target polynucleotide, said composition including a mixture of microparticles, wherein each microparticle has polynucleotides of the plurality attached thereto and wherein substantially all different polynucleotides in the plurality are attached to different microparticles.

b. Wang, EP 0304845 A2 (published 3/1/1989), throughout the application and especially at col. 3, lines 53-58, p. 4, lines 1-38, p. 5, lines 1-8 and 26-36 teach composition of matter comprising a plurality of polynucleotides that are fragments that are or complementary to target mRNA polynucleotides, said composition including a mixture of microparticles, wherein each microparticle has polynucleotides of the plurality attached thereto and wherein substantially all different polynucleotides in the plurality are attached to different microparticles.

c. In particular, Wang states:

> Thus the invention includes an embodiment wherein the mRNA molecules linked to the solid substrate include different kinds of target mRNA molecules to be assayed, which are assayed by contacting said solid substrate with an aqueous suspension of different varieties of microbeads, each different variety having linked thereto a corresponding different type of gene probe molecules, each type being capable of hybridizing with a particular one of said different kinds of mRNA molecules to be assayed, each variety of microbeads being differently labelled with different metal elements corresponding to each different type of gene probe molecules, thereby selectively linking corresponding, differently labelled microbeads to said different kinds of target mRNA molecules to be assayed which are linked to said solid substrate, and simultaneously and separately determining

the presence or quantity of the differently labelled microbeads by analysis of x-ray fluorescence characteristic of each different metal element.

Wang, at p. 4, line 57-p. 5., line 8. Thus Wang anticipates the invention of claim 5.

Claim Rejections - 35 U.S.C. § 103

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. Claims 5, 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang and further in view of Hornes et al., Patent No. 5,512,439, (applicant's reference P2, IDS filed 8/2/99).

a. Claims 5, 6 and 8 recites a composition of matter comprising a plurality of polynucleotides selected from cDNA molecules or fragments of a target polynucleotide, said composition including a mixture of microparticles, wherein each microparticle has polynucleotides of the plurality attached thereto and wherein substantially all different polynucleotides in the plurality are attached to different microparticles, wherein about 10^5 polynucleotides are attached to each of said microparticles, and wherein said plurality includes from ten to a hundred thousand cDNAs or fragments of a target polynucleotide.

b. **Wang**, EP 0304845 A2 (published 3/1/1989), throughout the application and especially at col. 3, lines 53-58, p. 4, lines 1-38, p. 5, lines 1-8 and 26-36 teach composition of matter comprising a plurality of polynucleotides that are fragments that are or complementary to target mRNA polynucleotides, said composition including a mixture of microparticles, wherein

each microparticle has polynucleotides of the plurality attached thereto and wherein substantially all different polynucleotides in the plurality are attached to different microparticles.

In particular, Wang states:

> Thus the invention includes an embodiment wherein the mRNA molecules linked to the solid substrate include different kinds of target mRNA molecules to be assayed, which are assayed by contacting said solid substrate with an aqueous suspension of different varieties of microbeads, each different variety having linked thereto a corresponding different type of gene probe molecules, each type being capable of hybridizing with a particular one of said different kinds of mRNA molecules to be assayed, each variety of microbeads being differently labelled with different metal elements corresponding to each different type of gene probe molecules, thereby selectively linking corresponding, differently labelled microbeads to said different kinds of target mRNA molecules to be assayed which are linked to said solid substrate, and simultaneously and separately determining the presence or quantity of the differently labelled microbeads by analysis of x-ray fluorescence characteristic of each different metal element.

Wang, at p. 4, line 57-p. 5., line 8.

c. Wang does not teach polynucleotides selected from cDNA molecules or wherein about 10^5 polynucleotides are attached to each of said microparticles, and said plurality includes from ten to a hundred thousand cDNAs or fragments of a target polynucleotide.

d. **Hornes et al.**, Patent No. 5,512,439, (applicant's reference P2, IDS filed 8/2/99), throughout the patent and especially at col. 5, lines 11-20 and 39-63, teach that all species of RNA are prone to rapid hydrolysis by ribonucleases present in cell lysates so that it is important that mRNA is isolated and reverse transcribed into cDNA as soon as possible after lysis; otherwise a significant fraction of the mRNA could be degraded. Hornes et al., disclose, that 10^3

to 10^6 probes (*i.e.*, complementary polynucleotides) may be "advantageously" attached to microbeads.

e. It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have made and used microparticles to which a plurality of cDNA polynucleotide molecules were attached, and wherein about 10^5 polynucleotides were attached to each of said microparticles, and wherein said plurality includes from ten to a hundred thousand cDNAs or fragments of a target polynucleotide.

f. One of ordinary skill in the art would have been motivated to make and use microparticles to which a plurality of cDNA polynucleotide molecules were attached, because Wang teaches microparticles to which a plurality of mRNA polynucleotide molecules were attached, and Hornes et al. teaches using cDNA in place of the mRNA from which it is reversed transcribed, so as to avoid degradation due to the well-known lability of mRNA. One of ordinary skill in the art would have been motivated to make and use microparticles to which 10^5 polynucleotides were attached to each of said microparticles, and wherein said plurality includes from ten to a hundred thousand cDNAs or fragments of a target polynucleotide, because Hornes et al. explicitly teach that 10^3 to 10^6 probes (*i.e.*, complementary polynucleotides) may be "advantageously" attached to microbeads.

Allowable Subject Matter

14. Claims 1-4 and 9-13 are allowable over the prior art. The prior art of record that is closest to that of the claimed invention are Chetverin et al., (applicant reference) and Dower et al. (applicant reference).

Claims 1-4 and 10-13 were allowed in Patent No. 5,654,413, of which the instant application is a reissue patent application, and are not amended in the instant reissue patent application. Claims 1-4 and 10-13 recite the limitation of "a minimally cross-hybridizing set."

Claim 9, which is dependent from claim 5, has been amended. However, claim 9 is free of the prior art because claim 9 recites the limitation "oligonucleotide tag" and the specification, at col. 6, lines 12-14, states: "Oligonucleotide tags of the invention each consist of a plurality of subunits 3 to 6 nucleotides in length selected from a minimally cross-hybridizing set."

Chetverin et al. and Dower et al. do not teach or fairly suggest oligonucleotide tags attached to solid phase supports wherein said tags comprise subunits selected from a minimally cross-hybridizing set, as contemplated by the specification col. 6-col. 9.

Chetverin et al. describe a method of sorting polynucleotides by hybridization to a binary oligonucleotide comprised of a constant region and a variable region. The variable regions of the repertoire of binary oligonucleotides comprise every possible sequence for an oligonucleotide of a given length. The polynucleotides to be sorted are prepared by attaching a fragment corresponding to the constant region of the binary oligonucleotide. Specific hybridization of a binary oligonucleotide to a prepared polynucleotide is effected by precise pairing of the constant

regions and the variable region of the oligonucleotide to a terminal region of the polynucleotide. The reference further teaches DNA sequencing of sorted DNA molecules. The reference does not teach or suggest attaching oligonucleotide tags as instantly claimed to the polynucleotides and identifying the polynucleotides of the subpopulation of tag-polynucleotide conjugates on the sole basis of the specifically hybridizing the oligonucleotide tags with their respective complements.

Dower et al., disclose compositions comprising a mixture of microparticles, each microparticle comprising polynucleotides of a population attached thereto such that substantially all different polynucleotides in the population are attached to different microparticles. Dower et al. does not disclose or suggest making or using polynucleotides selected from a minally cross-hybridizing set, as contemplated in the instant application.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mark L. Shibuya (SRC),* whose telephone number is (703) 308-9355, and/or to the patent analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.
16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader* may be reached at (703) 308-0447.
17. Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is (703) 308-0196.

Mark L. Shibuya
Patent Examiner
Technology Center 1600
April 3, 2001

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